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Eosinophils and Platelets: Players of the Game in Morbid Obese Boys with Metabolic Syndrome

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Abstract**—**Childhood obesity, which may lead to increased risk for heart diseases in children as well as adults, is one of the most important health problems throughout the world. Prevalences of morbid obesity and metabolic syndrome (MetS) are being increased during childhood age group. MetS is a cluster of metabolic and vascular abnormalities including hypercoagulability and an increased risk of cardiovascular diseases (CVDs). There are also some relations between some components of MetS and leukocytes. The aim of this study is to investigate complete blood cell count parameters that differ between morbidly obese boys and girls with MetS diagnosis. A total of 117 morbid obese children with MetS consulted to Department of Pediatrics in Faculty of Medicine Hospital at Namik Kemal University were included into the scope of the study. The study population was classified based upon their genders (60 girls and 57 boys). Their heights and weights were measured and body mass index (BMI) values were calculated. WHO BMI-for age and sex percentiles were used. The values above 99 percentile were defined as morbid obesity. Anthropometric measurements were performed. Waist-to-hip and head-to-neck ratios as well as homeostatic model assessment of insulin resistance (HOMA-IR) were calculated. Components of MetS (central obesity, glucose intolerance, high blood pressure, high triacylglycerol levels, low levels of high density lipoprotein cholesterol) were determined. Hematological variables were measured. Statistical analyses were performed using SPSS. The degree for statistical significance was $p \leq 0.05$. There was no statistically significant difference between the ages (11.2±2.6 years *vs* 11.2±3.0 years) and BMIs (28.6±5.2 kg/m^2 *vs* 29.3±5.2 kg/m^2) of boys and girls ($p \geq 0.05$), respectively. Significantly increased waist-to-hip ratios were obtained for boys (0.94±0.08 *vs* 0.91±0.06; p=0.023). Significantly elevated values of hemoglobin (13.55±0.98 *vs* 13.06±0.82; p=0.004), mean corpuscular hemoglobin concentration (33.79±0.91 *vs* 33.21±1.14; p=0.003), eosinophils (0.300±0.253 *vs* 0.196±0.197; p=0.014), and platelet (347.1±81.7 *vs* 319.0±65.9; p=0.042) were detected for boys. There was no statistically significant difference between the groups in terms of neutrophil/lymphocyte ratios as well as HOMA-IR values ($p \geq 0.05$). Statistically significant gender-based differences were found for hemoglobin as well as mean corpuscular hemoglobin concentration and hence, separate reference intervals for two genders should be considered for these parameters. Eosinophils may contribute to the development of thrombus in acute coronary syndrome. Eosinophils are also known to make an important contribution to mechanisms related to thrombosis pathogenesis in acute myocardial infarction. Increased platelet activity is observed in patients with MetS and these individuals are more susceptible to CVDs. In our study, elevated platelets described as dominant contributors to hypercoagulability and elevated eosinophil counts suggested to be related to the development of CVDs observed in boys may be the early indicators of the future cardiometabolic complications in this gender.

Keywords**—**Children, complete blood count, gender, metabolic syndrome.

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I. Introduction

THE pediatric obesity prevalence has increased a couple of times in recent years throughout the world. Childhood obesity, which may lead to the increased risk of CVDs both in children and adults, is one of the most important health problems in developed and developing countries. Obese children may be affected by factors such as severe medical as well as psychosocial problems and may also be associated with high morbidity and mortality risks in their adulthood period [1].

Increases in the prevalence of morbid obesity and MetS are being observed in pediatric age group. MetS is a clinical condition, which is associated with the increased risk of CVDs aside from various metabolic and vascular abnormalities encompassing also hypercoagulation.

Complete blood cell counts (CBCs) are components of hematological parameters and indicators of proinflammatory states. They appear to be associated also with MetS [2]. Obesity and factors related to MetS are not generally interpreted by evaluating a patient's CBCs [3].

Abdominal obesity is strongly correlated with cardiovascular risk. White blood cells (WBCs) have been widely investigated in adults as well as pediatric populations. Also, in adults, following bariatric surgery significant decreases in platelet (PLT) count was noted possibly mediated by weight loss [4]. However, there are few studies on some of WBC subpopulations, red blood cell (RBC) indices and PLTs performed on children and adolescents [2], [5], [6].

There are some relations between WBCs and MetS components. So far, gender differences were noted in thrombogenic profile associated to coronary obstruction [7]. Gender differences have also drawn great interest concerning various inflammatory markers in pediatric population [8]. However, any study investigating the possible differences between genders in terms of CBCs as well as their indices has not been reported in children with MetS yet. The aim of this study is the evaluation of hematological parameters on the basis of male as well as female genders in morbid obese (MO) children with MetS. This study was performed to detect any possible alterations between the genders in terms of WBCs and subpopulations, RBCs, PLTs and their indices during late-stage of obesity among children with MetS.

II. Patients and Methods

A. Patients

117 MO children with MetS (60 girls and 57 boys), aged between 6-18 years, consulted to Namik Kemal University, Medical Faculty Hospital, Department of Pediatrics, Outpatient Clinic were included into the scope of this study.

Weights and heights as well as systolic blood pressure, diastolic blood pressure values of the children were measured and recorded. Their BMI values were calculated. The other anthropometric measurements were performed. Waist-to-hip circumference as well as head-to-neck circumference ratios were calculated. Written informed consent forms were obtained from the parents of the children, who were admitted to the study. Namik Kemal University Medical Faculty Ethical Committee has approved the study protocol. The study has been carried out within the scope of Helsinki Declaration.

B. Obesity and MetS Criteria

The study population consists of MO children having MetS criteria. Children, whose age- and sex-dependent BMI values were greater than 99th percentiles, were accepted as MO. For the purpose of the obesity evaluation criteria, tables prepared by WHO and approved by Republic of Tuarkey, Ministry of Health were used [9]. Those with severe congenital abnormality and/or chronic disease were excluded from the scope of the study.

MetS was diagnosed based upon the criteria suggested by International Diabetes Federation [10].

In MO children having BMI values greater than 99th percentile,

1. Systolic and diastolic blood pressures above 130 and 85 mm Hg, respectively
2. Triacylglycerol (TRG) and high density lipoprotein cholesterol (HDL-C) concentrations above 150 mg/dl and/or below 40 mg/dl, respectively
3. Fasting blood glucose (FBG) levels above 100 mg/dl were considered as pathological values in terms of MetS.

Besides being MO, children having two pathological values of the above three-criteria-list were evaluated as MO+MetS.

C. Laboratory Analyses

Blood was drawn after 12 h of fasting. Fasting blood glucose was measured by spectrophotometric hexokinase assay; fasting insulin was detected by electro-chemiluminescence immunoassay.

High-sensitive C-reactive protein (*hs*CRP) analyses were performed using an immunological test system in a Roche COBAS C-501 chemistry analyzer.

The following equation was used to calculate homeostasis model assessment of insulin resistance (HOMA-IR) index [11], [12]: HOMA-IR= fasting glucose (mg/dL)*fasting insulin (µIU/ml)/ 22,5*0,0555

An automatic hematology analyzer [Pentra DX-Nexus (Horiba Medical ABX SAS, Japan)] was used for the determination of basic hematological parameters, as described elsewhere [13], in both gender groups of all children with MO+MetS. In this respect, the values related to erythrocytes and related indices [hemoglobin (HGB), hematocrit (HCT), erythrocyte count (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), erythrocyte distribution width (RDW)] + leukocytes and percents of leukocyte types [leukocyte count (WBC), polymorphonuclearleukocyte (neutrophil) (PMNL (N) %), lymphocyte (L) %, monocyte %, eosinophil %, basophil %] + PLTs and related indices [PLT count (PLT), PLT distribution width (PDW), mean PLT volume (MPV)] were obtained. N-to-L ratios were calculated. Potential statistically significant differences were investigated.

D. Statistical Analyses

SPSS 20 statistical package program for Windows was used for the statistical evaluation of the data obtained. The adequacy of the data to normal distribution was evaluated by Shapiro-Wilk test. To estimate statistically significant differences between the groups, t- and Mann-Whitney U tests were used for data exhibiting normal distribution and those that do not obey normal distribution, respectively. The values of parameters were tabulated as percentage and x±SD. $p \leq 0.05$ was the degree of statistical significance.

III. Results

Mean age values of girls (11.2±3.0 years) and boys (11.2±2.6 years) did not differ significantly between groups ($p \geq 0.05$). In a similar manner, any significant difference could not be observed between mean BMI values of the groups (29.3±5.2 kg/m^2 for girls and 28.6±5.2 kg/m^2 for boys).

Waist-to-hip circumference ratios in boys were statistically higher than those calculated for girls (0.94±0.08 *vs* 0.91±0.06; $p \leq 0.05$). There was no statistically significant difference between head-to-neck circumference ratios (1.65±0.23 in boys and 1.63±0.14 in girls, $p \geq 0.05$).

In Fig. 1, differences in terms of HGB as well as MCHC values of groups classified based upon gender were shown.

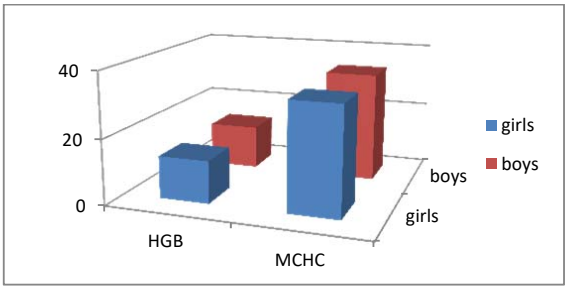

Fig. 1 Hemoglobin and mean corpuscular hemoglobin concentration values

The values related to eosinophile percentages of boys and girls were shown in Fig. 2. The values of PLT counts in boys and girls were demonstrated in Fig. 3.

Values obtained for eosinophil (0.300±0.253 *vs* 0.196±0.197; $p \leq 0.05$), HGB (13.55±0.98 *vs* 13.06±0.82; $p \leq 0.01$), MCHC (33.79±0.91 *vs* 33.21±1.14; $p \leq 0.01$) and PLT

(347.1±81.7 *vs* 319.0±65.9; p≤0.05) were statistically higher in boys.

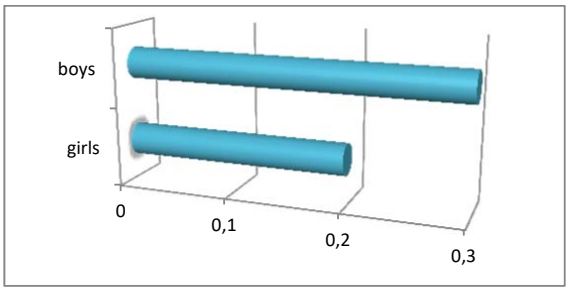

Fig. 2 Eosinophil percentage values of girls and boys

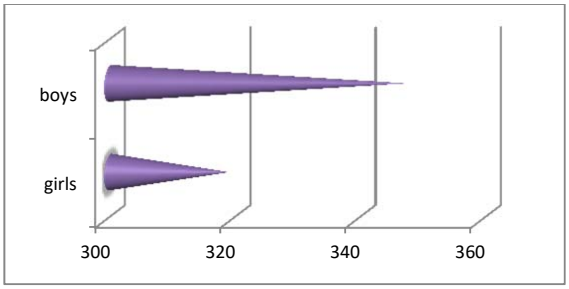

Fig. 3 PLT counts of girls and boys

Neither N-to-L ratios (1.60±0.93 in boys and 1.78±1.29 in girls) nor HOMA-IR (4.6±5.0 in boys and 4.2±3.5 in girls) values differed significantly between the groups of the genders (p≥0.05).

IV. Discussion

Increased leukocyte count is an independent risk factor for CVDs. Abdominal fat accumulation as well as hyperinsulinemia are also associated with atherosclerosis and trombogenic profile during which, elevations in leukocyte count are recorded. In a study, increased leukocyte, eosinophil and segmented neutrophil counts were reported in adolescents possessing excess body fat. Thrombocyte activation and aggregation are main events, which play some roles in the pathophysiology of CVDs [14]. Inflammation and thrombogenesis are introduced as potential causes of CVDs in patients with MetS [15].

There are some evidences on which, eosinophils may contribute to the development of thrombus in acute coronary syndrome [16]. It has also been reported that eosinophils make a significant contribution to thrombus pathogenesis in acute myocardial infarction [17].

Eosinophils are circulating in extremely low levels in blood of healthy individuals. Heart is a critical target organ in the presence of persistent hypereosinophilia. Since endothelial cells lining cardiac cavities are mainly the same as those lining blood vessels, similar mechanisms account for damages and dysfunctions detected in these cells.

Eosinophils expose the underlying tissues by damaging endothelial cells and activate natural extrinsic coagulation pathway. These cells also directly affect various factors involved in coagulation and increase tendency to thrombus formation in patients with hypereosinophilia. Cytotoxic and procoagulant properties of eosinophils are responsible from the development of cardiovascular complications in most of the hypereosinophilic patients. These patients also develop venous thrombosis. It is suggested that endothelial cell damage and thrombosis may progress faster in eosinophilic inflammation areas. Cardiovascular complications mediated by eosinophils are major determinants of hypereosinophilia-associated morbidity and mortality. In these patients, thrombosis may develop relatively early [18].

In a study performed on adults with MetS, eosinophil counts in men were reported statistically higher than those in women [15]. In our study, in MO children with MetS, statistically significantly higher eosinophil values were found in boys in comparison with in girls.

In a study reported from China, age-and sex-dependent BMI percentiles developed for Chinese children were used and children, whose percentiles are above 95 were considered as obese. In this study the number of boys is 2.5 times the number of girls. Also, the percentages of non-MetS children in both gender groups are 3 times the percentages of children with MetS. Medians of HOMA-IR values were calculated as 3.67 in the group without MetS findings and as 5.42 in the group with MetS [19].

Our study is organized on rarely observed MO children, whose percentiles are above 99. Upon evaluation of the numbers of MO children with MetS, almost the same number of girls and boys are found in groups. Our study is much more valuable from these points of view.

Increased PLT activity is observed in patients with MetS and these patients are more liable to CVDs. In a study, in which higher MPV is reported in patients with MetS compared to normal individuals, a correlation between this parameter and waist circumference were noted among the adults with abdominal obesity. Any differences couldn't be found in terms of PLT counts [20]. In our study, PLT counts are higher in boys in comparison with girls.

In a very recent study, it has been reported that HGB concentrations did not change with MetS parameters [21]. In our study performed on MO children with MetS, HGB values were greater in boys than in girls.

V. Conclusion

The differences based upon gender observed in both HGB and MCHC concentrations emphasize the need for the establishment of different reference intervals confined to boys as well as girls for these parameters.

Elevated PLT counts observed in this study are important, because PLTs are the major parameter contributing hypercoagulation. Also, in this study, it was concluded that elevated eosinophil count observed in boys, and also suggested to be associated with the development of CVDs, is introduced as an early indicator of cardiometabolic complications, which may be met in the future years in this gender.

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